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FILE 'CAPLUS' ENTERED AT 10:22:29 ON 14 SEP 2010

L10 3 S L9

L11 3 S L10 AND (PY<=2004 OR PRY<=2004 OR AY<=2004)

FILE 'REGISTRY' ENTERED AT 10:24:30 ON 14 SEP 2010 L12 STRUCTURE UPLOADED

L12 STRUCTURE UPLOADED

=> d 112

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L12 HAS NO ANSWERS

L12 STR

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FILE 'CAPLUS' ENTERED AT 10:25:00 ON 14 SEP 2010

L15 11 S L14

L16 9 S L15 AND (PY<=2004 OR PRY<=2004 OR AY<=2004)

L16 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN GI

AB Title compds. I [R1 = H, (un)substituted-alkyl, -cycloalkyl, etc.; R2 = H, (un)substituted-alkyl, -heterocyclyl, -aryl, etc.; R3 = H, CN, CO2H, (un)substituted alkyl or ester], and their pharmaceutically acceptable salts, are prepared and disclosed as antagonists of CGRP receptors. Thus, e.g., II was prepared by acylation of (3R,6S)-3-amino-1-(2-methoxyethyl)-6-phenylazepan-2-one (preparation given) with 4-nitrophenylchloroformate and subsequent amidation with 2-oxo-1-piperidinium-4-yl-2,3-dihydro-

Ι

1H-imidazo[4,5-b]pyridin-4-ium dichloride. I are useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. I possessed Ki or IC50 values of less than about 50 μM in CGRP receptor antagonist assays. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

2004:902378 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 141:379817

Preparation of piperidine derivatives as CGRP TITLE:

receptor

antagonists

Burgey, Christopher S.; Deng, Zhengwu J.; INVENTOR(S):

Nguyen, Diem

N.; Paone, Daniel V.; Shaw, Anthony W.;

Williams,

Theresa M.

Merck & Co., Inc., USA PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO	KIND DATE			APPLICATION NO.						DATE			
WO 2004092	A1		20041028		WO 2004-US11280								
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         781648-89-3P 781649-41-0P
          RL: PAC (Pharmacological activity); SPN (Synthetic preparation);
THU
          (Therapeutic use); BIOL (Biological study); PREP (Preparation);
USES
          (Uses)
               (drug candidate; preparation of heterocyclic piperidine derivs.
as CGRP
                receptor antagonists)
         781648-89-3 CAPLUS
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          1-Piperidinecarboxamide, N-[(3R,6S)-1-(cyanomethyl)hexahydro-2-
0x0-6-
          phenyl-1H-azepin-3-yl]-4-(2,3-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo-1H-imidazo[4,5-dihydro-2-oxo
b]pyridin-1-yl)-
              (CA INDEX NAME)
```

Absolute stereochemistry.

L16 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2010 ACS on STN

$$R^{1}-Y$$

$$R^{2}$$

$$R^{2}$$

$$R^{2}$$

$$R^{2}$$

AΒ The present invention relates to novel heterocyclic compds. that inhibit phosphodiesterase type 4 (PDE 4). The compds. are useful for treating inflammatory conditions, diseases of the central nervous systems and insulin resistant diabetes. Title compds. I [wherein R1 = independently H, (un) substituted alk(en/yn)yl, cyclo/cycloalkyl/aryl/heterocyclyl/heteroaryl/alkyl, cycloalkenyl, aryl, heterocyclyl, etc.; P = a bond, O, S, NR1; P1 = H, halo, OR1, S(:0)R1, C(:0)R1, NO2, etc.; R2 = H, halo, (un)substituted cyclo/alkyl, CN, CH:CH2 and derivs., OH and derivs., CO2H and derivs., etc.; A = (un) substituted aryl, saturated or unsatd. 5-7 membered heterocycle; and their analogs, tautomers, regioisomers, diastereoisomers, stereoisomers, geometrical isomers, N-oxides, polymorphs, and their pharmaceutically acceptable salts and pharmaceutically acceptable solvates] were prepared as phosphodiesterase type 4 (PDE4) inhibitors for treating inflammatory and allergic disorders (no data). For example, II was prepd via acylation of (3S)-3-aminoazolane-2,5-dione (preparation given) with 3-cyclopentyloxy-4-methoxybenzoyl chloride (preparation given), and alkylation of azolane intermediate with cyclopropylmethyl bromide in the presence of CsOH. I were found excellent PDE4 inhibitors in an in vitro study against human PDE4 enzyme (no data). I and their formulations are useful for the treatment of inflammatory allergic diseases, in particular bronchial asthma, allergic rhinitis and nephritis, as well as of diseases of the central nervous system and insulin resistant diabetes (no data).

ACCESSION NUMBER: 2004:220313 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 140:270743

TITLE: Preparation of heterocyclic amides, in

particular azolanes and pyridines as Phosphodiesterase IV

inhibitors for the treatment of inflammatory

(PDE4)

and

allergic disorders

INVENTOR(S): Thomas, Abraham; Bhavar, Prashant Kashinath;

Lingam,

(PDE4)

V. S. Prasada Rao; Joshi, Neelima Kairatkar

PATENT ASSIGNEE(S): Glenmark Pharmaceuticals Limited, India

SOURCE:

PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION N	O. DATE					
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GE, GH, GM, HR, HU,	ID, IL,	IN, IS,	JP, KE, KG, KP,	KR, KZ, LC,					
LK, LR,	I.V. MA.	MD. MG.	MK, MN, MW, MX,	MZ. NT. NO.					
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TM, TN,			SD, SE, SG, SK,						
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EE, ES, FI. FR. GB.	GR. HII.	TE. TT.	LU, MC, NL, PT,	RO. SE. ST.					
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IN 2002MU00804 20020904 <	A	20050121	IN 2002-MU804						
AU 2003263393 A1 20040329 AU 2003-263393 20030903 <									
PRIORITY APPLN. INFO.: IN 2002-MU804									
20020904 < WO 2003-IB3721 W									
20030903 < OTHER SOURCE(S): MARPAT 140:270743 IT &72883-3&-2P, (3S)-1-Cyanomethyl-3-[(3-cyclopentyloxy-4-									
<pre>methoxyphenylcarbonyl)amino]-2,5-dioxoazolane RL: PAC (Pharmacological activity); SPN (Synthetic preparation);</pre>									
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation);									
USES (Uses)									
(Phosphodiesterase IV inhibitor; preparation of heterocyclic									
amides, in particular azolanes and pyridines, as Phosphodiesterase IV									

inhibitors for treatment of inflammatory and allergic disorders) $\$

RN 672883-36-2 CAPLUS

CN Benzamide, N-[(3S)-1-(cyanomethyl)-2,5-dioxo-3-pyrrolidinyl]-3-(cyclopentyloxy)-4-methoxy- (CA INDEX NAME)

Absolute stereochemistry.

IT 672883-17-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation); RACT

(Reactant or reagent)

(intermediate; preparation of heterocyclic amides, in particular azolanes

and pyridines, as Phosphodiesterase IV (PDE4) inhibitors for treatment $\ensuremath{\mathsf{T}}$

of inflammatory and allergic disorders)

RN 672883-17-9 CAPLUS

CN Carbamic acid, [(3S)-1-(cyanomethyl)-2,5-dioxo-3-pyrrolidinyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 672883-37-3, (3S)-3-Amino-1-cyanomethylazolane-2,5-dione

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of heterocyclic amides, in particular azolanes and pyridines,

as Phosphodiesterase IV (PDE4) inhibitors for treatment of inflammatory $% \left(1\right) =\left(1\right) \left(1\right) +\left(1\right) \left(1\right) \left(1\right) +\left(1\right) \left(1\right)$

and allergic disorders)

RN 672883-37-3 CAPLUS

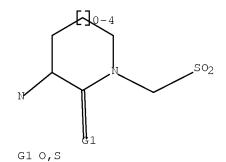
CN 1-Pyrrolidineacetonitrile, 3-amino-2,5-dioxo-, (3S)- (CA INDEX NAME)

L17

FILE 'REGISTRY' ENTERED AT 10:28:16 ON 14 SEP 2010 STRUCTURE UPLOADED

L17 STRUCTURE UPLOADED

=> d 117 L17 HAS NO ANSWERS L17 STR



1 S L17 SSS SAM L19 6 S L17 SSS FULL

FILE 'CAPLUS' ENTERED AT 10:28:50 ON 14 SEP 2010

L20 2 S L19

L21 2 S L20 AND (PY<=2004 OR PRY<=2004 OR AY<=2004)

L21 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2010 ACS on STN $\mbox{\rm GI}$

AB A rapid structure-activity study was performed by parallel liquid synthesis on N,N'-disubstitution of 3-aminoazepin-2-one to afford potent and specific farnesyl transferase inhibitors with low nM

enzymic and cellular activities. The activities of the selected compds. were validated in vivo, and compds. I (R = 2-C1, 3-Br) presented significant antitumor activity.

ACCESSION NUMBER: 2003:462563 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 140:42082

TITLE: Parallel liquid synthesis of N, N'-

disubstituted

3-aminoazepin-2-ones as potent and specific

farnesyl

transferase inhibitors

AUTHOR(S): Le Diguarher, Thierry; Ortuno, Jean-Claude;

Dorey,

Gilbert; Shanks, David; Guilbaud, Nicolas;

Pierre,

Alain; Fauchere, Jean-Luc; Hickman, John A.;

Tucker,

Gordon C.; Casara, Patrick J.

CORPORATE SOURCE: Department of Medicinal Chemistry, Institut de

Recherches Servier, Croissy sur Seine, 78290,

Fr.

SOURCE: Bioorganic & Medicinal Chemistry (2003),

11(14), 3193-3204

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:42082

IT 635753-78-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation);

BIOL

(Biological study); PREP (Preparation)

(N,N'-disubstituted 3-aminoazepin-2-ones as farnesyl

transferase

inhibitors)

RN 635753-78-5 CAPLUS

CN Benzonitrile, 4-[[5-[[[hexahydro-2-oxo-1-[(phenylsulfonyl)methyl]-

1H-

azepin-3-yl]amino]methyl]-1H-imidazol-1-yl]methyl]-, hydrochloride

(1:2)

(CA INDEX NAME)

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IT 635754-80-2P 635754-85-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT

(Reactant or reagent)

(N,N'-disubstituted 3-aminoazepin-2-ones as farnesyl

transferase

inhibitors)

RN 635754-80-2 CAPLUS

CN Carbamic acid, [hexahydro-2-oxo-1-[(phenylsulfonyl)methyl]-1H-azepin-3-yl]-

, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 635754-85-7 CAPLUS

CN 2H-Azepin-2-one, 3-aminohexahydro-1-[(phenylsulfonyl)methyl]- (CA INDEX

NAME)

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OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE

THIS RECORD

(7 CITINGS)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

L21 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2010 ACS on STN $\mbox{\rm GI}$

$$\begin{array}{c} & & & \\ & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

Title compds. I [W = CO, CH2; X = bond, alkylene, CO, S(O)n,AΒ S(0) nA1, COA1, A1S(0) nA2, A1COA2; Y = (un) substituted aryl, heteroaryl, cycloalkyl, heterocyclalkyl; T = NR1, NR1CO; V = H, (un) substituted aryl, heteroaryl; A1, A2 = alkylene; A3 = (CR2R3)p; R1-R3 = H, (un)substituted alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; n = 0-2; p = 0-4] were prepared for use as farnesyl transferase inhibitors in the treatment of cancers, neurofibromatosis type 1, and restenosis after angioplasty or vascular surgery. Thus, (S)-3-amino-1-benzyl-2-azepanone was prepared from L-lysine in 4 steps and treated with 1-(4cyanobenzyl)-1H-imidazole-5- carboxaldehyde, obtained by treating HOCH2COCH2OH with PhCH2NH2 and KSCN and oxidation of the resulting alc., to give the title compound II.

ACCESSION NUMBER: 2002:555454 CAPLUS Full-text

DOCUMENT NUMBER: 137:125097

TITLE: Novel azepanes as farnesyl transferase

inhibitors

INVENTOR(S): Casara, Patrick; Le Diguarher, Thierry; Dorey,

Gilbert; Hickman, John; Pierre, Alain; Tucker,

Gordon;

Guilbaud, Nicolas; Ortuno, Jean-Claude;

Fauchere,

Jean-Luc

PATENT ASSIGNEE(S): Les Laboratoires Servier, Fr.

PCT Int. Appl., 78 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: French

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO 2002057223					A2		20020725		1	WO 2002-FR147						
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OM, PH,
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                                           AU 2002-231886
20020116 <--
PRIORITY APPLN. INFO.:
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20010118 <--
                                            WO 2002-FR147
20020116 <--
OTHER SOURCE(S):
                        MARPAT 137:125097
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(Biological
     study); PREP (Preparation); USES (Uses)
        (novel azepanes as farnesyl transferase inhibitors)
RN
     443920-50-1 CAPLUS
     Benzonitrile, 4-[[5-[[(3S)-hexahydro-2-oxo-1-
[(phenylsulfonyl)methyl]-1H-
     azepin-3-yl]amino]methyl]-1H-imidazol-1-yl]methyl]- (CA INDEX
NAME)
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Absolute stereochemistry.

FILE 'REGISTRY' ENTERED AT 10:30:00 ON 14 SEP 2010

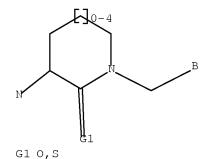
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L22

L25



L23 0 S L22 SSS SAM L24 4 S L22 SSS FULL

> FILE 'CAPLUS' ENTERED AT 10:30:31 ON 14 SEP 2010 1 S L24

L25 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2010 ACS on STN The epimerization-free synthesis and characterization of a class AΒ of conformational constrained lactam aminoboronic acid inhibitors of dipeptidyl peptidase IV (DPP IV; E.C. 3.4.14.5) is described. These compds. have the advantage that they cannot undergo the pHdependent cyclization prevalent in most dipeptidyl boronic acids that attenuates their potency at physiol. pH. For example, D-3-boroAla), one of the best lactam inhibitors of DPP IV, is several orders of magnitude less potent than L-Ala-L-boroPro, as measured by Ki values (2.3 nM vs 30 pM, resp.). At physiol. pH, however, it is actually more potent than L-Ala-L-boroPro, as measured by IC50 values (4.2 nM vs 1400 nM), owing to the absence of the potency-attenuating cyclization. In an interesting and at first

sight surprising reversal of the relationship between stereochem. and potency observed with the conformational unrestrained XaaboroPro class of inhibitors, the L-L diastereomers of the lactams are orders of magnitude less effective than the D-L lactams. However, this interesting reversal and the unexpected potency of the D-L lactams as DPP IV inhibitors can be understood in structural terms, which is explained and discussed here.

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DOCUMENT NUMBER: 147:95888

TITLE: Synthesis and characterization of constrained

peptidomimetic dipeptidyl peptidase IV

inhibitors:

amino-lactam boroalanines

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IT 942216-61-7P 942216-62-8P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

methionine and homoserine derivs. via coupling with boroamino acid

derivs. as key step, and their antidiabetic activity as $\mbox{\sc dipeptidyl}$

peptidase IV inhibitor)

RN 942216-61-7 CAPLUS

CN Boronic acid, B-[(1R)-1-[(3R)-3-amino-2-oxo-1-pyrrolidinyl]ethyl]-

hydrochloride (1:1) (CA INDEX NAME)

● HCl

RN 942216-62-8 CAPLUS
CN Boronic acid, B-[(1R)-1-[(3S)-3-amino-2-oxo-1-pyrrolidinyl]ethyl],
hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

L26

FILE 'REGISTRY' ENTERED AT 10:31:37 ON 14 SEP 2010 STRUCTURE UPLOADED

L26 STRUCTURE UPLOADED

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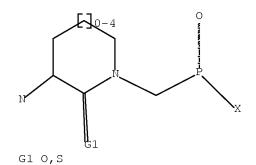
L27

0 S L26 SSS SAM

L28 0 S L26 SSS FULL L29 STRUCTURE UPLOADED

L29 STRUCTURE UPLOADED

=> d 129 L29 HAS NO ANSWERS L29 STR



L30 0 S L29 SSS SAM L31 0 S L29 SSS FULL